EUROPEAN UROLOGY 67 (2015) 612–616

available at www.sciencedirect.com
journal homepage: www.europeanurology.com

Platinum Priority – Brief Correspondence

*Editorial by Jacob M. Patterson and Nicholas J. Rukin on pp. 617–618 of this issue*

# Systematic Review and Meta-analysis of the Clinical Effectiveness of Shock Wave Lithotripsy, Retrograde Intrarenal Surgery, and Percutaneous Nephrolithotomy for Lower-pole Renal Stones

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**Article info**

***Article history:***
Accepted September 27, 2014

***Keywords:***
Nephrolithiasis
Urolithiasis
Kidney stones
Lithotripsy
Shock wave lithotripsy
Extracorporeal shock wave lithotripsy
Ureterorenoscopy
Retrograde intrarenal surgery
Percutaneous nephrolithotomy

**Abstract**

The prevalence of urolithiasis is increasing. Lower-pole stones (LPS) are the most common renal calculi and the most likely to require treatment. A systematic review comparing shock wave lithotripsy (SWL), retrograde intrarenal surgery (RIRS), and percutaneous nephrolithotomy (PNL) in the treatment of ≤20 mm LPS in adults was performed. Comprehensive searches revealed 2741 records; 7 randomised controlled trials (RCTs) recruiting 691 patients were included. Meta-analyses for stone-free rate (SFR) at ≤3 mo favoured PNL over SWL (risk ratio [RR]: 2.04; 95% confidence interval [CI], 1.50–2.77) and RIRS over SWL (RR: 1.31; 95% CI, 1.08–1.59). Stone size subgroup analyses revealed PNL and RIRS were considerably more effective than SWL for >10 mm stones, but the magnitude of benefit was markedly less for ≤10 mm stones. The quality of evidence (Grading of Recommendations Assessment, Development, and Evaluation [GRADE]) for SFR was moderate for these comparisons. The median SFR from reported RCTs suggests PNL is more effective than RIRS. The findings regarding other outcomes were inconclusive because of limited and inconsistent data. Well-designed, prospective, comparative studies that measure these outcomes using standardised definitions are required, particularly for the direct comparison of PNL and RIRS. This systematic review, which used Cochrane methodology and GRADE quality-of-evidence assessment, provides the first level 1a evidence for the management of LPS.

***Patient summary:*** We thoroughly examined the literature to compare the benefits and harms of the different ways of treating kidney stones located at the lower pole. PNL and RIRS were superior to SWL in clearing the stones within 3 mo, but we were unable to make any conclusions regarding other outcomes. More data is required from reliable studies before firm recommendations can be made.

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The prevalence of urolithiasis is increasing [1]. Lower-pole stones (LPS), defined as stones lying within a lower (inferior) pole calyx, are the most common renal stones. LPS are more likely to require treatment because they are less likely to pass spontaneously. The treatment of LPS is controversial, especially ≤20 mm stones [2], with competing interventions possessing advantages and disadvantages. Treatment options include percutaneous nephrolithotomy (PNL), retrograde intrarenal surgery (RIRS), or shock wave lithotripsy (SWL).

http://dx.doi.org/10.1016/j.eururo.2014.09.054
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We performed a systematic review and meta-analysis to compare the benefits and harms of PNL, RIRS, and SWL in the treatment of LPS (≤20 mm) in adults. Only randomised controlled trials (RCTs) were included, and Cochrane Collaboration standards and Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines were strictly followed (Supplement 1). The primary outcome was stone-free rate (SFR) at ≤3 mo. Risk of bias (RoB) and Grading of Recommendations Assessment, Development, and Evaluation (GRADE) assessments were performed to appraise the quality of the evidence (level 1a) synthesised.

The search identified 2741 records, which were doubly screened, and 21 articles were scrutinised for eligibility. Twelve articles reporting on 7 RCTs recruiting a total of 691 patients were included (PRISMA diagram; Supplementary Fig. 1). Baseline characteristics and intervention protocols are summarised in Supplementary Tables 1 and 2. RoB assessment findings included low risk of selection, attrition, and reporting biases in most studies (Supplementary Fig. 2). Two studies reported industry funding [3–5].

Table 1 summarises the study findings. GRADE quality assessment was moderate for SFR of RIRS versus SWL and PNL versus RIRS but was low or very low for all other outcomes (Supplementary Table 3). Meta-analysis was possible only for the outcome of SFR for PNL versus SWL and RIRS versus SWL (Fig. 1) because of clinical heterogeneity.

**Table 1 – Summary of results**

| | Study ID | Outcome | No. of patients | | Value, % (*n*) | | RR (95% CI)* | *p* value* |
|---|---|---|---|---|---|---|---|---|
| | | | PNL | SWL | PNL | SWL | | |
| PNL vs SWL | Albala et al [3] | SFR (3 mo), ≤20 mm | 48 | 45 | 95.8 (46) | 40 (18) | 2.40 (1.67–3.44) | <0.00001 |
| | | SFR (3 mo), 1–10 mm | 20 | 19 | 100 (20) | 63.6 (12) | 1.56 (1.11–2.21) | 0.01 |
| | | SFR (3 mo), 11–20 mm | 28 | 26 | 92.9 (26) | 23.1 (6) | 4.02 (1.98–8.18) | 0.0001 |
| | | Unplanned procedures | 49 | 55 | 2 (1) | 20 (10) | 0.11 (0.01–0.85) | 0.03 |
| | | Retreatment | 49 | 55 | 6.1 (3) | 14.5 (8) | 0.42 (0.12–1.50) | 0.18 |
| | | *Hospital stay, 0–30 mm* | 49 | 55 | 2.66 d | 0.55 d | Unavailable** | <0.0001 |
| | Yuruk et al [10] | SFR (3 mo), ≤20 mm | 31 | 31 | 96.7 (30) | 54.8 (17) | 1.76 (1.27–2.44) | 0.0006 |
| | | Unplanned procedures | 31 | 31 | 0 (0) | 3.2 (1) | 0.33 (0.01–7.88) | 0.50 |
| | | Retreatment | 31 | 31 | 0 (0) | 9.7 (3) | 0.14 (0.01–2.66) | 0.19 |
| | | Complications | 31 | 31 | 6.5 (2) | 6.5 (2) | 1.00 (0.15–6.66) | 1.00 |
| | | | RIRS | SWL | RIRS | SWL | | |
| RIRS vs SWL | Pearle et al [5] | SFR (3 mo), ≤10 mm | 32 | 26 | 72 (23) | 65 (17) | 1.10 (0.77–1.57) | 0.60 |
| | | Unplanned procedures | 32 | 26 | 3.1 (1) | 7.7 (2) | 0.41 (0.04–4.23) | 0.45 |
| | | Retreatment | 32 | 26 | 3.1 (1) | 11.5 (3) | 0.27 (0.03–2.45) | 0.25 |
| | | Complications, postop | 33 | 30 | 21 (7) | 23 (7) | 0.91 (0.36–2.29) | 0.84 |
| | | Procedure time, min ± SD | NR | NR | 90.4 ± 43.8 | 66.5 ± 27.9 | Unavailable** | 0.01** |
| | | Hospital stay | 35 | 32 | 0.06 d | 0 d | Unavailable** | 0.68** |
| | Salem et al [7] | SFR (3 mo), ≤20 mm | 30 | 30 | 96.7 (29) | 56.7 (17) | 1.71 (1.24–2.35) | 0.001 |
| | | Complications | 30 | 30 | 16.7 (5) | 23.3 (7) | 0.71 (0.25–2.00) | 0.52 |
| | Kumar et al [6] | SFR ≤20 mm (3 mo) | 90 | 90 | 86.6 (78) | 66.6 (60) | 1.30 (1.10–1.54) | 0.002 |
| | | SFR <10 mm (3 mo) | 49 | 53 | 87.7 (43) | 71.7 (38) | 1.22 (1.00–1.49) | 0.05 |
| | | SFR 10–20 mm (3 mo) | 41 | 37 | 85.4 (35) | 59.5 (22) | 1.44 (1.07–1.93) | 0.02 |
| | | Unplanned procedures | 90 | 90 | 17.7 (16) | 21.1 (19) | 0.84 (0.46–1.53) | 0.57 |
| | | Retreatment | 90 | 90 | 1.1 (1) | 67.1 (60) | 0.02 (0.00–0.12) | <0.0001 |
| | | Complications | 90 | 90 | 11.1 (10) | 6.6 (6) | 1.67 (0.63–4.39) | 0.30 |
| | Sener et al [8] | SFR <10 mm (3 mo) | 70 | 70 | 100 (70) | 91.5 (64) | 1.09 (1.01–1.18) | 0.02 |
| | | Unplanned procedures | 70 | 70 | 0 (0) | 1.4 (1) | 0.33 (0.01–8.04) | 0.50 |
| | | Retreatment | 70 | 70 | 0 (0) | 8.6 (6) | 0.08 (0.00–1.34) | 0.08 |
| | | Complications | 70 | 70 | 2.8 (3) | 5.7 (4) | 0.75 (0.17–3.23) | 0.70 |
| | Singh et al [9] | SFR (1 mo) 10–20 mm | 35 | 35 | 85.7 (30) | 54.3 (19) | 1.58 (1.13–2.20) | 0.007 |
| | | Unplanned procedures | 35 | 35 | 0 (0) | 5.7 (2) | 0.20 (0.01–4.02) | 0.29 |
| | | Retreatment | 35 | 35 | 14.3 (5) | 45 (16) | 0.31 (0.13–0.76) | 0.01 |
| | | Complications | 35 | 35 | 31.4 (11) | 48.6 (17) | 0.65 (0.36–1.17) | 0.15 |
| | | | RIRS | PNL | RIRS | PNL | | |
| PNL vs RIRS | Kuo et al [4] | SFR (3 mo), 11–25 mm | 13 | 15 | 45.6 (6)*** | 66.7 (10)*** | 1.44 (0.73–2.87) | 0.29 |
| | | Secondary Rx | NR | NR | 25.0% | 9.1% | Unavailable** | 0.59** |
| | | Complications | NR | NR | 0.0% | 6.7% | Unavailable** | 0.999** |
| | | Hospital stay, d | NR | NR | 0 | 2.8 ± 2.2 | Unavailable** | <0.001** |
| | | Procedure time, min ± SD | NR | NR | 125 ± 49 | 111 ± 38 | Unavailable** | NS** |
| | | Mean recovery, d ± SD | NR | NR | 10.0 ± 7.7 | 23.5 ± 20.5 | Unavailable** | <0.05** |

CI = confidence interval; NR = not reported; NS = not significant; PNL = percutaneous nephrolithotomy; RIRS = retrograde intrarenal surgery; RR = risk ratio; Rx = treatment; SFR = stone-free rate; SWL = shock wave lithotripsy.
* RR, 95% CI, and associated *p* values were calculated from primary study data where possible.
** Insufficient data reported for calculation. Where possible, reported *p* values are stated. No RRs were reported.
*** Numerators were not reported. These are estimates using reported percentages and denominators.

Overall median SFRs (≤20 mm) favoured PNL (96.3%) over RIRS (91.7%) and over SWL (54.5%) (Supplementary Table 4). No studies reported economic outcomes.

Five RCTs compared RIRS versus SWL [5–9]. Meta-analysis showed a higher SFR for RIRS (89.5% vs 70.5%). Subgroup analyses revealed that RIRS was considerably more effective than SWL for 10–20 mm stones. but the magnitude of benefit was markedly less for ≤10 mm stones. RIRS had a numerically lower unplanned procedure rate, albeit not statistically significant. Outcomes for retreatment rates were inconsistent, reflecting different retreatment thresholds. Complication rates were not significantly different.

Pearle et al [5] (<10 mm LPS) found SWL conferred superior quality of life, shorter convalescence, and fewer analgesic requirements than RIRS. Conversely, Singh et al [9] (10- to 20-mm LPS) reported significantly higher satisfaction

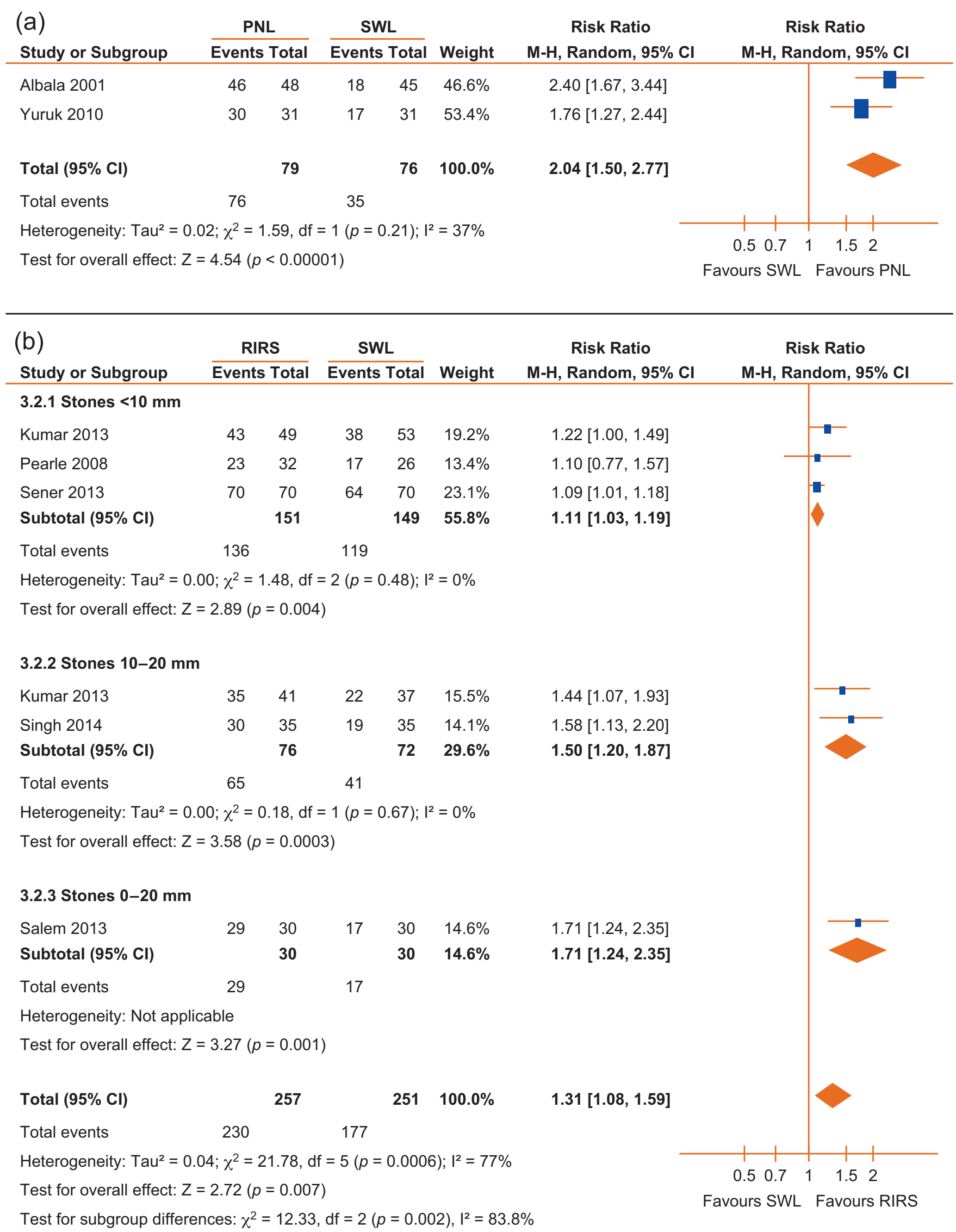


**Fig. 1 – Forest plot demonstrating meta-analysis of stone-free rates at ≤3 mo for lower-pole renal stones ≤20 mm: (a) percutaneous nephrolithotomy (PNL) versus shock wave lithotripsy (SWL); (b) retrograde intrarenal surgery (RIRS) versus SWL (including subanalyses for ≤10 mm [3.2.1], 10–20 mm [3.2.2], and ≤20 mm [total]). Salem et al (2013) [7], Sener et al (2014) [8], and Singh et al (2014) [9] defined *stone free* (SF) as fragments ≤3 mm. Kumar et al (2013) [6], Albala et al (2001) [3], and Yuruk et al (2010) [10] did not define SF. Pearle et al (2008) [5] reported SF rate (SFR; 50% vs 35%, *p* = 0.25) and SFR plus <4 mm fragments; the latter was considered as the SFR in this review. All studies reported SFR at 3 mo, except Singh et al [9], who reported SFR at 1 mo. Salem et al [7] did not report outcomes by stone size but stated that "stone size (<10 mm) correlated with SF status" for SWL but not RIRS.**
**CI = confidence interval; M-H = Mantel-Haenszel test; PNL = percutaneous nephrolithotomy; RIRS = retrograde intrarenal surgery; SWL = shock wave lithotripsy.**

with RIRS and comparable convalescence ( $p = 0.36$) for three or fewer SWL sessions, although in cases for which only a single SWL session was required, convalescence was shorter ( $p = 0.0001$).

There were conflicting data on patients' willingness to undergo the procedure again. Pearle et al [5] favoured SWL (63% vs 90%, $p = 0.031$), whereas Singh et al [9] favoured RIRS (84% vs 50%, $p = 0.002$). Singh et al [9] reported significantly worse voiding symptoms ( $p = 0.026$) following RIRS (which included routine stent placement). Procedural duration favoured SWL in the study by Pearle et al [5] ( $p = 0.01$) but favoured RIRS in the study by Singh et al [9] ( $p = 0.1434$); however, patients requiring only one SWL session had a shorter operative duration ( $p = 0.0001$). Singh et al [9] reported a shorter hospital stay for those with three or fewer sessions of SWL ( $p = 0.0001$).

Two RCTs directly compared PNL and SWL. Intervention protocols differed slightly, including number of sessions. *Stone free* (SF) was not defined. Meta-analysis suggested a benefit for PNL (96.2% vs 46.1%). Albala et al [3] stratified SFRs by stone size, suggesting that the magnitude of benefit of PNL was lower for ≤10 mm stones versus 11–20 mm stones. Both studies found a numerically lower rate of retreatment for PNL, albeit not significant. Unplanned procedure rates were inconsistent, although event rates were low. There was heterogeneity in what constituted retreatment or an unplanned procedure, and intervention thresholds were not defined.

Complications were reported only by Yuruk et al [10] and were neither defined nor categorised. Albala et al [3] reported Short Form-36 health surveys for 0–30 mm stones; no significant differences were demonstrated between PNL and SWL. Yuruk et al [10] reported more scintigraphic scarring following SWL (16.1% vs 3.2%, $p = 0.13$). No patient demonstrated decreased renal function.

One study that reported initial results only compared PNL and RIRS [4]. There was no significant difference in SFR, although PNL had a longer hospital stay and mean recovery duration.

A 2009 Cochrane review on nephrolithiasis [1] in any location included only two of the seven RCTs in this review, did not incorporate GRADE assessment, and found no difference in SFR between RIRS and SWL for LPS. Present European Association of Urology urolithiasis guidelines recommend SWL or RIRS for <10 mm LPS. For 10–20 mm LPS, treatment should depend "on favourable and unfavourable factors" including anatomic factors; however, two identified RCTs [3,6] found that anatomic factors did not affect SFR following SWL. Present guidelines are not based on a robust systematic review and do not include either RoB or appraisal of quality of evidence.

The major limitation of this review is the paucity of evidence for the comparison of PNL versus RIRS and the lack of reliable evidence concerning outcomes other than SFR. Reporting of patient-focused outcomes (including length of stay, analgesic requirement, and quality of life) and economic outcomes was poor. These data are critical to inform clinicians' and patients' decision making. Well-designed RCTs that measure these outcomes in a standardised manner are required, particularly for PNL and RIRS. Ideally, studies should account for confounding factors including stone size, ancillary procedures, heterogeneity of interventions, and thresholds of retreatment.

This systematic review, performed using Cochrane review methodology and incorporating RoB and GRADE assessment, provides the first level 1a evidence for the management of LPS. SFRs were highest following PNL; however, PNL is the most invasive intervention and requires the longest hospital stay. It has been suggested that PNL is associated with higher morbidity and convalescence. Our review was unable to support firm conclusions regarding these associations, but morbidity and convalescence may be reduced with recent modifications (eg, *tubeless* or *mini-perc*) [2].

RIRS offers higher SFRs than SWL, which is the least effective in terms of stone clearance, particularly for 10–20 mm LPS. However, SWL is the least invasive intervention, possibly with the shortest convalescence and the highest acceptability to patients, for whom multiple sessions are not required. Ultimately, until gaps in the evidence base are addressed, especially regarding PNL versus RIRS, treatment decisions should be influenced by patients' individual characteristics and expectations and by the available clinical expertise and facilities.

***Author contributions:*** James F. Donaldson had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

*Study concept and design:* Donaldson, Lardas, Scrimgeour, Lam, McClinton.
*Acquisition of data:* Donaldson, Lardas, Scrimgeour, Stewart, MacLennan.
*Analysis and interpretation of data:* Donaldson, Lardas, Scrimgeour, Stewart, MacLennan, Lam, McClinton.
*Drafting of the manuscript:* Donaldson, Lardas.
*Critical revision of the manuscript for important intellectual content:* Donaldson, Lardas, Scrimgeour, Stewart, MacLennan, Lam, McClinton.
*Statistical analysis:* Donaldson, Lardas, MacLennan, Lam.
*Obtaining funding:* None.
*Administrative, technical, or material support:* Stewart.
*Supervision:* MacLennan, Lam, McClinton.
*Other* (specify): None.

***Financial disclosures:*** James F. Donaldson certifies that all conflicts of interest, including specific financial interests and relationships and affiliations relevant to the subject matter or materials discussed in the manuscript (eg, employment/affiliation, grants or funding, consultancies, honoraria, stock ownership or options, expert testimony, royalties, or patents filed, received, or pending), are the following: None.

***Funding/Support and role of the sponsor:*** None.

## Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.eururo.2014.09.054.

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